10/523,184

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TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 05	CASREACT(R) - Over 10 million reactions available
NEWS 4	DEC 14	2006 MeSH terms loaded in MEDLINE/LMEDLINE
NEWS 5	DEC 14	2006 MeSH terms loaded for MEDLINE file segment of TOXCENTER
NEWS 6	DEC 14	CA/CAplus to be enhanced with updated IPC codes
NEWS 7	DEC 21	IPC search and display fields enhanced in CA/CAplus with the IPC reform
NEWS 8	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 9	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 10	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 11	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 12	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 13	JAN 30	Saved answer limit increased
NEWS 14	JAN 31	Monthly current-awareness alert (SDI) frequency added to TULSA

NEWS EXPRESS	JANUARY 03 CURRENT VERSION FOR WINDOWS IS V8.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 USERS CAN OBTAIN THE UPGRADE TO V8.01 AT http://download.cas.org/express/v8.0-Discover/
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:05:20 ON 10 FEB 2006

=> ile reg
ILE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

```
=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 13:05:29 ON 10 FEB 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    8 FEB 2006  HIGHEST RN 873837-20-8
DICTIONARY FILE UPDATES:   8 FEB 2006  HIGHEST RN 873837-20-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10523184\10523184.str
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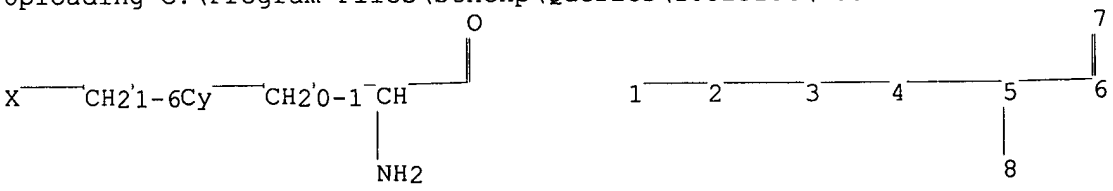


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chain nodes :
1  2  3  4  5  6  7  8
chain bonds :
1-2  2-3  3-4  4-5  5-6  5-8  6-7
exact/norm bonds :
2-3  3-4  5-8  6-7
exact bonds :
1-2  4-5  5-6


Match level :
1:CLASS  2:CLASS  3:Atom  4:CLASS  5:CLASS  6:CLASS  7:CLASS  8:CLASS
```
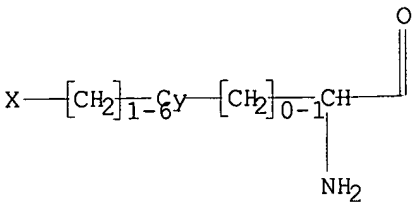

Generic attributes :
3:
Saturation : Unsaturated

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 13:05:57 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 61144 TO ITERATE

3.3% PROCESSED 2000 ITERATIONS 1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1208151 TO 1237609
PROJECTED ANSWERS: 280 TO 942

L2 1 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 13:06:13 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1223921 TO ITERATE

81.7% PROCESSED 1000000 ITERATIONS 39 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.16

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1223921 TO 1223921
PROJECTED ANSWERS: 39 TO 67

L3 39 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 167.38 167.59

FILE 'CAPLUS' ENTERED AT 13:06:40 ON 10 FEB 2006

FILE COVERS 1907 - 10 Feb 2006 VOL 144 ISS 8
FILE LAST UPDATED: 9 Feb 2006 (20060209/ED)

=> s l3
L4 15 L3

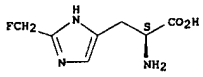
=> d ibib abs hitstr tot

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1242590 CAPLUS
DOCUMENT NUMBER: 144:2014
TITLE: Modulating pH-sensitive binding using non-natural amino acids
INVENTOR(S): Datta, Deepshikha; Goddard, William A.; Tirrell, David; Peng, Joyce Yaochun
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005260711	A1	20051124	US 2005-94625	20050330
PRIORITY APPLN. INFO.:			US 2004-557541P P	20040330

AB The invention provides methods, systems and reagents for regulating pH-sensitive protein interaction by incorporating non-natural amino acids into the protein (e.g. an antibody, or its functional fragment, derivative, etc.). The invention also relates to specific uses in regulating pH-sensitive binding of antibodies to tumor site, by conferring enhanced tumor-specificity/selectivity. In that embodiment, the non-natural amino acids preferably have desirable side-chain pKa's, such that at below physiol. pH (e.g. about pH 6.3-6.5) the non-natural amino acid confer enhanced binding to tumor antigens in acidic environments. Such non-natural amino acids can be incorporated by any suitable means, such as by utilizing a modified aminoacyl-tRNA synthetase to charge the nonstandard amino acid to a modified tRNA, which forms strict Watson-Crick base-pairing with a codon that normally forms wobble base-pairing with natural tRNAs (e.g. the degenerate codon orthogonal system).
IT **869849-99-0 869850-00-0 869850-01-1**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulating pH-sensitive binding using non-natural amino acids)
RN 869849-99-0 CAPLUS
CN L-Histidine, 2-(fluoromethyl)- (9CI) (CA INDEX NAME)

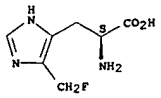
Absolute stereochemistry.



RN 869850-00-0 CAPLUS
CN L-Histidine, 5-(fluoromethyl)- (9CI) (CA INDEX NAME)

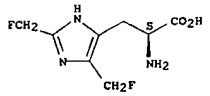
Absolute stereochemistry.

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 869850-01-1 CAPLUS
CN L-Histidine, 2,5-bis(fluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

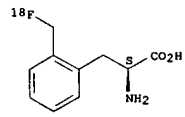


L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1124679 CAPLUS
DOCUMENT NUMBER: 142:70833
TITLE: Radioactively labelled amino acid analogues, their preparation and use
INVENTOR(S): Mertens, John J. R.
PATENT ASSIGNEE(S): Mallinckrodt Inc., USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

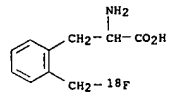
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110500	A1	20041223	WO 2003-US24436	20030801
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2494704	AA	20041223	CA 2003-2494704	20030801
EP 1539250	A1	20050615	EP 2003-816986	20030801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			EP 2002-78228	A 20020802
			WO 2003-US24436	W 20030801

OTHER SOURCE(S): MARPAT 142:70833
AB The present invention relates to Halogenated amino acid analogs for use in diagnosis, which compds. have the general formula X-(CH2)n-R(CH2)m-CH(NH2)-CO2H wherein : R is (C1-C6) alkyl optionally substituted with thioether or ether oxygen atom when n = 0, or a substituted aromatic or heterarom. ring when n = 1-6; and m = 0 or 1; and X is a halogen atom. The invention further relates to precursor compds. for these analogs, to a method of preparing these analogs, to a pharmaceutical composition comprising these analogs and to the use of these analogs and compns. in the diagnosis of cancer.
IT **813446-50-3 813446-51-4 813446-52-5**
813446-53-6 813446-54-7 813446-55-8
813446-56-9 813446-57-0 813446-58-1
813446-59-2 813446-60-5 813446-61-6
813446-62-7 813446-63-8 813446-64-9
813446-65-0 813446-66-1 813446-67-2
813446-68-3
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(radiolabeled amino acid analogs as imaging agents)
RN 813446-50-3 CAPLUS
CN L-Phenylalanine, 2-(fluoro-18F-methyl)- (9CI) (CA INDEX NAME)

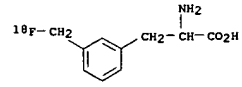
L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Absolute stereochemistry.



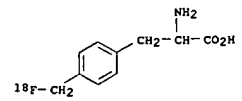
RN 813446-51-4 CAPLUS
CN Phenylalanine, 2-(fluoro-18F-methyl)- (9CI) (CA INDEX NAME)



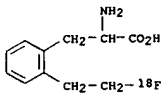
RN 813446-52-5 CAPLUS
CN Phenylalanine, 3-(fluoro-18F-methyl)- (9CI) (CA INDEX NAME)



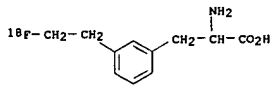
RN 813446-53-6 CAPLUS
CN Phenylalanine, 4-(fluoro-18F-methyl)- (9CI) (CA INDEX NAME)



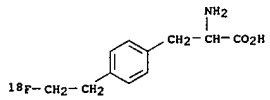
RN 813446-54-7 CAPLUS
CN Phenylalanine, 2-[2-(fluoro-18F)ethyl]- (9CI) (CA INDEX NAME)



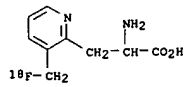
RN 813446-55-8 CAPLUS
CN Phenylalanine, 3-[2-(fluoro-18F)ethyl]- (9CI) (CA INDEX NAME)



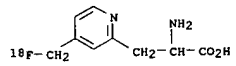
RN 813446-56-9 CAPLUS
CN Phenylalanine, 4-[2-(fluoro-18F)ethyl]- (9CI) (CA INDEX NAME)



RN 813446-57-0 CAPLUS
CN 2-Pyridinepropanoic acid, α-amino-3-(fluoro-18F-methyl)- (9CI) (CA INDEX NAME)

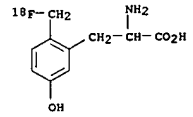


RN 813446-58-1 CAPLUS
CN 2-Pyridinepropanoic acid, α-amino-4-(fluoro-18F-methyl)- (9CI) (CA INDEX NAME)

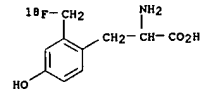


RN 813446-59-2 CAPLUS

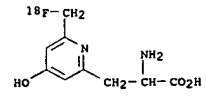
RN 813446-64-9 CAPLUS
CN Phenylalanine, 2-(fluoro-18F-methyl)-5-hydroxy- (9CI) (CA INDEX NAME)



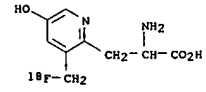
RN 813446-65-0 CAPLUS
CN Tyrosine, 2-(fluoro-18F-methyl)- (9CI) (CA INDEX NAME)



RN 813446-66-1 CAPLUS
CN 2-Pyridinepropanoic acid, α-amino-6-(fluoro-18F-methyl)-4-hydroxy- (9CI) (CA INDEX NAME)

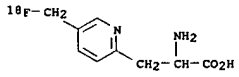


RN 813446-67-2 CAPLUS
CN 2-Pyridinepropanoic acid, α-amino-3-(fluoro-18F-methyl)-5-hydroxy- (9CI) (CA INDEX NAME)

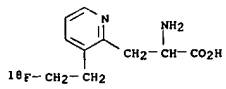


RN 813446-68-3 CAPLUS
CN Phenylalanine, 3-[2-(fluoro-18F)ethyl]-5-hydroxy- (9CI) (CA INDEX NAME)

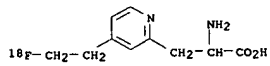
CN 2-Pyridinepropanoic acid, α-amino-5-(fluoro-18F-methyl)- (9CI) (CA INDEX NAME)



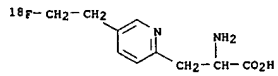
RN 813446-60-5 CAPLUS
CN 2-Pyridinepropanoic acid, α-amino-3-[2-(fluoro-18F)ethyl]- (9CI) (CA INDEX NAME)



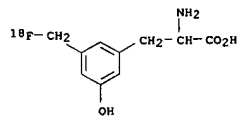
RN 813446-61-6 CAPLUS
CN 2-Pyridinepropanoic acid, α-amino-4-[2-(fluoro-18F)ethyl]- (9CI) (CA INDEX NAME)

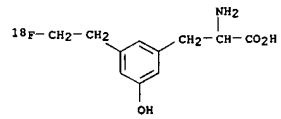


RN 813446-62-7 CAPLUS
CN 2-Pyridinepropanoic acid, α-amino-5-[2-(fluoro-18F)ethyl]- (9CI) (CA INDEX NAME)



RN 813446-63-8 CAPLUS
CN Phenylalanine, 3-(fluoro-18F-methyl)-5-hydroxy- (9CI) (CA INDEX NAME)





REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:404935 CAPLUS
DOCUMENT NUMBER: 131:59136
TITLE: Pyridones as Src family SH2 domain inhibitors
INVENTOR(S): Betageri, Rajashekhar; Beaulieu, Pierre L.; Llinas-Brunet, Montse; Ferland, Jean-Marie; Cardozo, Mario; Moss, Neil; Patel, Usha; Proudfoot, John R.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 172 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

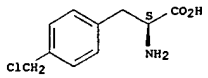
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931066	A1	19990624	WO 1998-US26123	19981209
W: AU, BG, BR, BY, CA, CN, CZ, EE, HU, IL, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SK, TR, UA, UZ, VN				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2315113	AA	19990624	CA 1998-2315113	19981209
AU 9917194	A1	19990705	AU 1999-17194	19981209
US 6054470	A	20000425	US 1998-208113	19981209
EP 1045836	A1	20001025	EP 1998-962022	19981209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LT, LV, FI, RO				
JP 2003514762	T2	20030422	JP 2000-538993	19981209
ZA 9811570	A	19990916	ZA 1998-11570	19981217
US 6268365	B1	20010731	US 1999-438629	19991112
US 6284768	B1	20010904	US 1999-438647	19991112
US 6156784	A	20001205	US 1999-455633	19991207

PRIORITY APPLN. INFO.: US 1997-69971P P 19971218
US 1998-208113 A3 19981209
WO 1998-US26123 W 19981209
US 1999-129414P P 19990415

OTHER SOURCE(S): MARPAT 131:59136
AB Compds. A-Q-NB-CH(D-NH-E)-CH2-a-R-C (ring a is selected from cycloalkyl, aryl, heterocyclyl; A = alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, heterocyclyl, aryl; Q = CO, SO2, C:S; B = H, alkyl, a nitrogen-protecting group; R = bond, alkyl, aryl, heterocyclyl, cycloalkyl linker; C is an acidic functionality that carries one or two neg. charges at physiol. pH; D = CH2, CO, C:S; E are certain six-membered unsatd. heterocycles) were prepared These compds. possess the ability to disrupt the interaction between regulatory proteins possessing one or more SH2 domains and their native ligands. Thus, 3-[2'(S)-(1''''-naphthylacetyl)amino-3'-[4''-(1'''-carboxy-1'''-methylethyl)benzene]propanoylamino]-1-(4-methoxybenzyl)-4-methyl-2-pyridone was prepared and showed IC50 = 96 μM for blocking IL-2 production in human blood CD4 pos. T-lymphocytes after T cell receptor and CD28 crosslinking.
IT **228411-62-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(pyridones as Src family SH2 domain inhibitors)

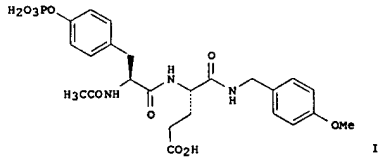
L4 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 228411-62-9 CAPLUS
CN L-Phenylalanine, 4-(chloromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:261309 CAPLUS
DOCUMENT NUMBER: 131:67637
TITLE: Ligands for the Tyrosine Kinase p56lck SH2 Domain: Discovery of Potent Dipeptide Derivatives with Monocharged, Nonhydrolyzable Phosphate Replacements
AUTHOR(S): Beaulieu, Pierre L.; Cameron, Dale R.; Ferland, Jean-Marie; Gauthier, Jean; Ghiro, Elise; Gillard, James; Gorys, Vida; Poirier, Martin; Rancourt, Jean; Wernic, Dominik; Llinas-Brunet, Montse; Betageri, Raj; Cardozo, Mario; Hickey, Eugene R.; Ingraham, Richard; Jakes, Scott; Kabcenell, Alisa; Kirrane, Tom; Lukas, Susan; Patel, Usha; Proudfoot, John; Sharma, Rajiv; Tong, Liang; Moss, Neil
CORPORATE SOURCE: Bio-Mega Research Division, Boehringer Ingelheim (Canada) Ltd., Laval, QC, H7S 2G5, Can.
SOURCE: Journal of Medicinal Chemistry (1999), 42(10), 1757-1766
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

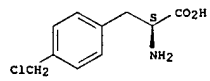


I

AB P56lck is a member of the src family of tyrosine kinases. Through modular binding units called SH2 domains, p56lck promotes phosphotyrosine-dependent protein-protein interactions and plays a critical role in signal transduction events that lead to T-cell activation. Starting from the phosphorylated dipeptide (I), a high-affinity ligand for the p56lck SH2 domain, novel dipeptides were designed that contain monocharged, nonhydrolyzable phosphate group replacements and bind to the protein with KD's in the low micromolar range. Replacement of the phosphate group in phosphotyrosine-containing sequences by a (R/S)-hydroxyacetic or an oxamic acid moiety leads to hydrolytically stable, monocharged ligands, with 83- and 233-fold decreases in potency, resp. This loss in binding affinity can be partially compensated for by incorporating large lipophilic groups at the inhibitor N-terminus. These groups provide up to 13-fold increases in potency depending on the nature of the phosphate replacement. The discovery of potent (2-3 μM), hydrolytically stable dipeptide derivs., bearing only two charges at physiol. pH, represents a significant step toward the discovery of compds. with cellular activity and the development

L4 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
of novel therapeutics for conditions assocd. with undesired T-cell proliferation.
IT **134790-19-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(design and preparation of dipeptide derivs. as ligands for binding to tyrosine kinase p56lck SH2 domain)
RN 134790-19-5 CAPLUS
CN L-Phenylalanine, 4-(chloromethyl)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

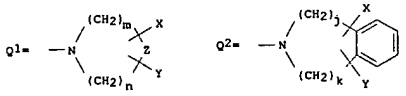
REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:746209 CAPLUS
DOCUMENT NUMBER: 126:19324
TITLE: Preparation of arylsulfonylamino acid amide trypsin and thrombin inhibitors.
INVENTOR(S): Hoyle, William; Howarth, Graham Arton; Brundish, Derek
Edward; Kane, Peter Daniel; Walker, Clive Victor; Hayler, Judy; Fullerton, Joseph David; Smith, Garric Paul; Wathey, William Bernard; et al.
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9629327	A1	19960926	WO 1996-GB520	19960308
W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9648872	A1	19961008	AU 1996-48872	19960308
EP 815103	A1	19980107	EP 1996-904963	19960308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 11502219	T2	19990223	JP 1996-528155	19960308
ZA 9602112	A	19960918	ZA 1996-2112	19960315

PRIORITY APPLN. INFO.: GB 1995-5538 A 19950318
WO 1996-GB520 W 19960308

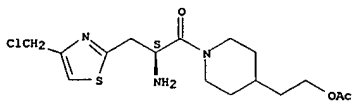
OTHER SOURCE(S): MARPAT 126:19324
GI



AB ArSO2AQ [Ar = (substituted) aryl, heterocyclyl; A = amino acid residue; Q = Q1, Q2; X = H, alkyl; Y = SO3H, PO(OR14)2, OH, SH, NR15R16, halo, (substituted) (CqH2q)Q3, etc.; Q3 = H, COR14, CO2R14, CONR15R16, SO3H, OR14, OCOR14, PO(OR14)2, NR15R16, SR14, halo; R14, R15, R16 = H, alkyl, cycloalkyl, aralkyl; R15R16N = 5-6 membered azacycloalkyl, oxazacycloalkyl; XY = O; Z = bond, O, N optionally substituted by X or Y; m, n = 2-4; m + n = 4-6, j, k = 0-2; j + k = 2-3; when A = Arg, then X, Y = alkyl; when Q = COR14, then q = 1-8], were prepared Thus, (S)-arginine and 3-(1-methyl-1-phenylethyl)benzenesulfonyl chloride were stirred with Na2CO3 in H2O/dioxane to give 5-guanidino-2(S)-[3-(1-methyl-1-

L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
phenylethyl)benzenesulfonylamino]pentanoic acid. The latter was converted to the acid chloride hydrochloride, which was condensed with pyrrolidin-2(R)-ylmethanol in DMF contg. Et3N to give N-[4-guanidino-1(S)-2(R)-hydroxymethylpyrrolidine-1-carbonylbutyl]-3-(1-methyl-1-phenylethyl)benzenesulfonamide. Tested title compds. inhibited human α-thrombin with Ki = 0.007-0.094 μM.
IT 184043-62-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of arylsulfonylamino acid amide trypsin and thrombin inhibitors)
RN 184043-62-7 CAPLUS
CN 4-Piperidineethanol, 1-[2-amino-3-[4-(chloromethyl)-2-thiazolyl]-1-oxopropyl]-, acetate (ester), monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L4 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:609917 CAPLUS
DOCUMENT NUMBER: 125:248492
TITLE: Preparation of peptides and compounds that bind to SH2 (src homology region 2) domains of proteins and methods for their identification
INVENTOR(S): Patel, Dinesh V.; Gordeev, Mikhail F.; Gordon, Eric; Grove, J. Russell; Hart, Charles P.; Kim, Moon H.; Szardenings, Anna Katrin
PATENT ASSIGNEE(S): Affymax Technologies N.V., Neth.
SOURCE: PCT Int. Appl., 204 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

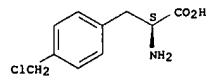
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9623813	A1	19960808	WO 1996-US1544	19960131
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
AU 9649720	A1	19960821	AU 1996-49720	19960131

PRIORITY APPLN. INFO.: US 1995-382100 A 19950201
WO 1996-US1544 W 19960131

AB SH2-binding peptides comprising a core sequence of amino acids Z7XZ8X (X = a member independently selected from the group consisting of the 20 genetically coded L-amino acids and the stereoisomeric D-amino acids; Z7 = phosphotyrosine or an isostere thereof; Z8 = asparagine or an isostere thereof; the amino acid terminus is acylated; the peptide is less than 14 amino acids; provided that if Z7 is phosphotyrosine and Z8 is asparagine, then the peptide is not GDGZ7XZ8XPLL), which bind to the SH2 domain or domains of various proteins, are prepared These peptides and compds. have application as agonists and antagonists of SH2 domain containing proteins, and as diagnostic or. A library of peptides bound to a solid support, useful for identifying ligands capable of binding to SH2 domains, is also prepared therapeutic agents for the diagnosis or treatment of disease conditions. A method for identifying an SH2-binding peptide comprises contacting the resp. members of a library with an SH2 domain containing protein or SH2 domain fragment and identifying SH2-binding peptides on the basis of a binding affinity of ≤1 + 10-4 M. In particular, a method for treating a disease associated with aberrant cell growth, differentiation, or regulation which is associated with defects in receptor tyrosine kinase pathways comprises administering to a patient above peptide in an amount sufficient to partially block or inhibit a cellular signal transduction pathway. Said disease is selected from cancer, developmental and

L4 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
differentiation disease, and insulin-resistant (or non-insulin dependent) diabetes. Thus, a phosphotyrosine-contg. peptide library on a solid support with the general sequence A-pY-X1-X2-X3-S-V (pY = phosphotyrosine residue, X1 - X3 = Ala, Arg, Asn, Asp, Glu, Gln, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Val, Tyr, Trp, Vvl, Nle, etc.) representing 17,576 peptides was prepd. and one of the library sequence (ApYLNESV) showed greater affinity for the SH2 domain than did the pos. control sequence (ApYINQSV, residue from the SH2-binding domain of human EGF) (4.5 μM vs. 12 μM).
IT 134790-19-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides and peptide library having binding affinity to SH2 domains for diagnosis and treatment of diseases)
RN 134790-19-5 CAPLUS
CN L-Phenylalanine, 4-(chloromethyl)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L4 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:186168 CAPLUS
DOCUMENT NUMBER: 124:230163
TITLE: Streptogramins and method for preparing same by mutasynthesis
INVENTOR(S): Blanc, Veronique; Thibaut, Denis; Bamas-Jacques, Nathalie; Blanche, Francis; Crouzet, Joel; Barriere, Jean-Claude; Debussche, Laurent; Famechon, Alain; Paris, Jean-Marc; Dutruc-Rosset, Gilles
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer S.A., Fr.
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

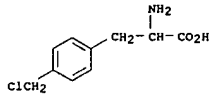
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9601901	A1	19960125	WO 1995-FR889	19950704
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, UG, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2722210	A1	19960112	FR 1994-8478	19940708
FR 2722210	B1	19960814		
CA 2193130	AA	19960125	CA 1995-2193130	19950704
AU 9528912	A1	19960209	AU 1995-28912	19950704
AU 712397	B2	19991104		
EP 770132	A1	19970502	EP 1995-924396	19950704
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 1152338	A	19970618	CN 1995-194026	19950704
JP 10502532	T2	19980310	JP 1995-504149	19950704
HU 77341	A2	19980330	HU 1997-42	19950704
BR 9508714	A	19980602	BR 1995-8714	19950704
RU 2205183	C2	20030527	RU 1997-101899	19950704
ZA 9505688	A	19960226	ZA 1995-5688	19950707
NO 9700047	A	19970107	NO 1997-47	19970107
US 6352839	B1	20020305	US 1997-765907	19970320
US 2002142947	A1	20021003	US 2001-987614	20011115
US 6833382	B2	20041221		

PRIORITY APPLN. INFO.:

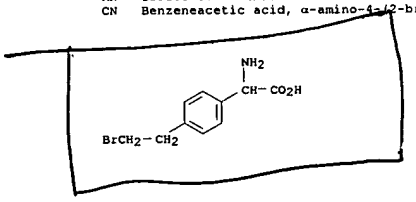
FR 1994-8478	A	19940708
WO 1995-FR889	W	19950704
US 1997-765907	A3	19970320

AB Novel group B streptogramin-like compds. and a method for preparing streptogramins by mutasynthesis using a mutated micro-organism to influence the biosynthesis of at least one of the precursors of group B streptogramines, are disclosed. Novel nucleotide sequences involved in the biosynthesis of said precursors, and their uses, are also disclosed. Genes papB, papC, pipA, snbF, and hpaA of Streptomyces pristinaespiralis were cloned and sequenced. S. pristinaespiralis mutants containing an inactivated papA, pipA, or hpaA gene were prepared The papA- mutant cultured in the presence of phenylalanine derivs. (synthesis given) was used to prepare pristinamycin derivs.
IT **174733-12-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(streptogramins and their manufacture with Streptomyces mutants)

L4 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 174733-12-1 CAPLUS
CN Phenylalanine, 4-(chloromethyl)- (9CI) (CA INDEX NAME)

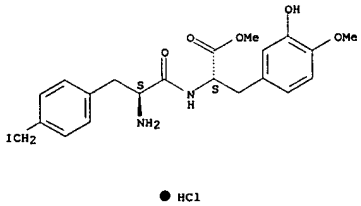


L4 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:701249 CAPLUS
DOCUMENT NUMBER: 121:301249
TITLE: The synthesis of D,L-p-vinylphenylglycine by amidoalkylation, and its reactions
AUTHOR(S): Sheffer-Dee-Noor, Shani; Ben-Ishai, Dov
CORPORATE SOURCE: Dep. Chem., Tech.-Israel Inst. Technol., Haifa, 32000, Israel
SOURCE: Tetrahedron (1994), 50(23), 7009-18
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 121:301249
AB Amidoalkylation of (2-chloroethyl)benzene or (2-bromoethyl)benzene with α-hydroxyglycine derivs. RCONHCH(OH)CO2H (R = Ph, MeO), followed dehydrohalogenation, affords N-protected p-vinylphenylglycines RCONHCH(C6H4CH:CH2-4)CO2R1 (I; R1 = H, Me). Transformation of the vinyl group in I (R = MeO) leads to derivs. MeO2CNHCH(C6H4R2-4)CO2R1 (R2 = CHBrCH2Br, CO2H, CHMeSPh, CHMeOAc, CHMeNHCO2Me, CH2OH, CHO, oxiranyl). The deprotection of these compds. is described.
IT **159106-07-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and elimination of, vinylglycine from)
RN 159106-07-7 CAPLUS
CN Benzeneacetic acid, α-amino-4-(2-bromoethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:217059 CAPLUS
DOCUMENT NUMBER: 120:217059
TITLE: Total synthesis of (+)-piperazinomycin. [Erratum to document cited in CA120(9):106615r]
AUTHOR(S): Boger, Dale L.; Zhou, Jiacheng
CORPORATE SOURCE: Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: Journal of the American Chemical Society (1994), 116(4), 1601
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The errors were not reflected in the abstract or the index entries.
IT **152429-83-9P**
RL: PREP (Preparation)
(intermediate in total synthesis of piperazinomycin (Erratum))
RN 152429-83-9 CAPLUS
CN L-Tyrosine, 3-hydroxy-N-[4-(iodomethyl)-L-phenylalanyl]-O-methyl-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

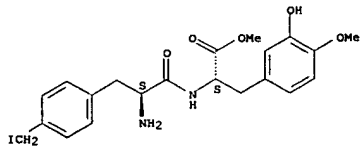
Absolute stereochemistry.



● HCl

IT **152429-93-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of (Erratum))
RN 152429-93-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-N-[4-(iodomethyl)-L-phenylalanyl]-O-methyl-, methyl ester (9CI) (CA INDEX NAME)

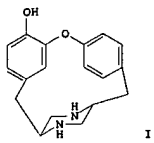
Absolute stereochemistry.



L4 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L4 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:106615 CAPLUS
DOCUMENT NUMBER: 120:106615
TITLE: Total synthesis of (+)-Piperazinomycin
AUTHOR(S): Boger, Dale L.; Zhou, Jiacheng
CORPORATE SOURCE: Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: Journal of the American Chemical Society (1993), 115(24), 11426-33
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:106615
GI



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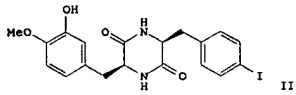
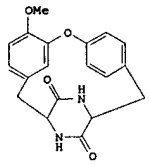


II



III

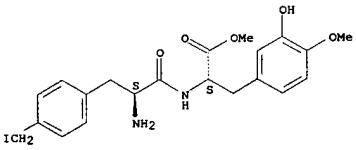
AB A concise total synthesis of (+)-piperazinomycin (I), a novel naturally occurring macrocyclic piperazine possessing antimicrobial and antifungal activity, is detailed on the basis of the implementation of an improved Ullmann macrocyclization reaction conducted on a diketopiperazine II to give diazatetracycloheneicosahexaene III (53%).

IT **152429-83-9P**
RL: PREP (Preparation)
(intermediate in total synthesis of piperazinomycin)

RN 152429-83-9 CAPLUS
CN L-Tyrosine, 3-hydroxy-N-[4-(iodomethyl)-L-phenylalanyl]-O-methyl-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

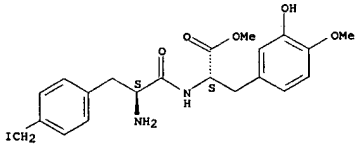


● HCl

IT **152429-93-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 152429-93-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-N-[4-(iodomethyl)-L-phenylalanyl]-O-methyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

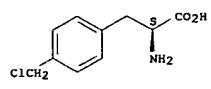
ACCESSION NUMBER: 1993:517789 CAPLUS
DOCUMENT NUMBER: 119:117789
TITLE: Synthesis of human CCK26-33 and CCK-33 related analogs on 2,4-DMBHA and TMBHA
AUTHOR(S): Miranda, Maria Teresa Machini; Liddle, Rodger A.; Rivier, Jean E.
CORPORATE SOURCE: Clayton Found. Lab. Pept. Biol., Salk Inst. Biol. Stud., La Jolla, CA, 92037, USA
SOURCE: Journal of Medicinal Chemistry (1993), 36(12), 1681-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB New analogs of human cholecystokinin (CCK) in which the sulfotyrosine was replaced by p-(sulfomethyl)phenylalanine [Phe(p-CH2SO3Na)], methionines by norleucines, and tryptophan by L-2-naphthylalanine (Nal) were prepared to increase the chemical stability of the peptides during the synthesis, full deprotection/cleavage, and purification steps. Thus, modified title CCK analogs R-Asp-Phe(p-CH2SO3Na)-Nle-Gly-Nal-Nle-Asp-Phe-NH2 [R = H (I), H-Lys-Ala-Pro-Ser-Gly-Arg-Nle-Ser-Ile-Val-Lys-Asn-Leu-Gln-Asn-Leu-Asp-Pro-Ser-His-Arg-Ile-Ser-Asp-Arg (II)] were prepared by 9-fluorenylmethoxycarbonyl (Fmoc) solid phase methodol. on two different resins [2,4-dimethoxybenzhydrylamine (2,4-DMBHA) and 4-(benzyloxy)-2',4'-dimethoxybenzhydrylamine (TMBHA)]. While the syntheses on the TMBHA resin was more sluggish than those carried out on the 2,4-DMBHA resin, both final crude products were of equivalent relative purity and after purification gave approx. the same final yields of analogs estimated to have a purity >93% using reverse-phase HPLC and capillary zone electrophoresis. I and II were further characterized by amino acid anal. and liquid secondary ion mass spectrometry. II was submitted to 33 Edman cycles and shown to be the desired product with <3% preview. Both analogs were tested for their ability to stimulate amylase release from isolated rat pancreatic acini. In this assay, I and II were 10 and 30 times less potent than CCK-8, resp.

IT **134790-19-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and substitution of, with sulfite, sulfomethyl derivative from)

RN 134790-19-5 CAPLUS
CN L-Phenylalanine, 4-(chloromethyl)-, hydrochloride (9CI) (CA INDEX NAME)

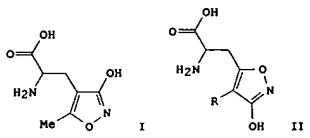
Absolute stereochemistry.



● HCl

L4 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

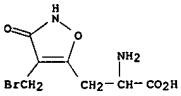
L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:571987 CAPLUS
DOCUMENT NUMBER: 117:171987
TITLE: Excitatory amino acid receptor ligands. Synthesis and biological activity of 3-isoxazolol amino acids structurally related to homoibotenic acid
AUTHOR(S): Christensen, Inge T.; Ebert, Bjarke; Madsen, Ulf; Nielsen, Birgitte; Brehm, Lotte; Krogsgaard-Larsen, Povl
CORPORATE SOURCE: PharmaBiotec Res. Cent., R. Dan. Sch. Pharm., Copenhagen, DK-2100, Den.
SOURCE: Journal of Medicinal Chemistry (1992), 35(19), 3512-19
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 117:171987
GI



I II

AB The 3-isoxazolol amino acid (RS)-2-amino-3-(3-hydroxy-5-methylisoxazol-4-yl)propionic acid (AMPA) (I) and the isomeric compound (RS)-2-amino-3-(3-hydroxy-4-methylisoxazol-5-yl)propionic acid (4-methylhomoibotenic acid (II, R = Me) are potent agonists at the AMPA subtype of central excitatory amino acid receptors. Using II (R = Me) as a lead structure, the amino acids II (R = n-Bu, n-octyl, CH2CH2OH), in which the 4-Me group of II (R = Me) is replaced by substituents of different size and polarity, were synthesized. Attempts to synthesize 4-(bromomethyl)homoibotenic acid (II, R = CH2Br), a potential receptor alkylating agent, were unsuccessful. II (R = n-Bu, CH2CH2OH) were equipotent as inhibitors of [3H]AMPA binding (IC50 = 2 μM) and showed similar excitatory activity in the rat cortical slice preparation I (R = n= octyl) did not show significant affinity for AMPA receptor sites, but turned out to be a weak N-methyl-D-aspartic acid (NMDA) receptor antagonist. However, like II (R = n-Bu, CH2CH2OH), II (R = n-octyl) did not significantly affect the binding of the competitive NMDA antagonist, [3H]CPP, or the noncompetitive NMDA antagonist, [3H]MK-801. None of the amino acids II showed detectable affinity for [3H]kainic acid binding sites. Like the parent compound, II (R = Me) (IC50 = 0.18 μM), II (R = n-Bu), (IC50 = 0.18 μM), II (R = CH2CH2OH) (IC50 = 0.14 μM), and in particular II (R = n-octyl) (IC50 = 0.02 μM) were effective inhibitors of calcium chloride-dependent [3H]glutamic acid binding, whereas AMPA is inactive (IC50 > 100 μM) in this binding assay. Thus, II (R = n-octyl) is an effective and highly selective

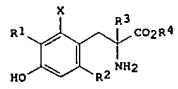
L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
inhibitor of calcium chloride-dependent [3H]glutamic acid binding and may be a useful tool for studies of the physiol. relevance and pharmacol. importance of this binding affinity.
IT **143006-76-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(attempted preparation of)
RN 143006-76-2 CAPLUS
CN 5-Isoxazolepropanoic acid, α-amino-4-(bromomethyl)-2,3-dihydro-3-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:106792 CAPLUS
DOCUMENT NUMBER: 116:106792
TITLE: Preparation of fluoromethyltyrosine compounds as tyrosine hydroxylase inhibitors
INVENTOR(S): McDonald, Ian A.; Jung, Michel J.; Sabol, Jeffrey S.
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals, Inc., USA
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

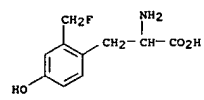
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 451422	A1	19911016	EP 1990-401022	19900413
R: FR				
PRIORITY APPLN. INFO.:			EP 1990-401022	19900413

OTHER SOURCE(S): MARPAT 116:106792
GI



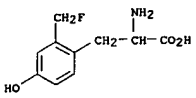
I

AB The title compds. (I; X = CH2F, CHF2; R1, R2 = H, F, Cl, Br, iodo; one of R1, R2 = halo and the other = H; R3 = H, Me; R4 = H, alkyl, Ph, PhCH2 when X = CHF2; R4 = H when X = CH2F), useful in the treatment of diseases caused by high levels of catecholamines such as hypertension, schizophrenia, and pheochromocytoma, are prepared Thus, bromination of N,O-di-tert-butoxycarbonyl-2-(fluoromethyl)tyrosine Me ester with N-bromosuccinimide and fluorination of the resulting bromide with AgF gave, after deprotection, 2-fluoromethyltyrosine (II). Injection of mice with II (unspecified amount) i.p. reduced the cortical norepinephrine level to 63 ± 6% of the control vs. 58 ± 9% for α-methyl-p-tyrosine.
IT **133409-90-2P 139241-95-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as tyrosine hydroxylase inhibitor)
RN 133409-90-2 CAPLUS
CN Tyrosine, 2-(fluoromethyl)- (9CI) (CA INDEX NAME)



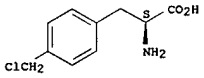
RN 139241-95-5 CAPLUS

L4 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN Tyrosine, 2-(fluoromethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● HCl

L4 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:450275 CAPLUS
DOCUMENT NUMBER: 115:50275
TITLE: Solid-phase synthesis of a fully active analog of cholecystokinin using the acid-stable Boc-Phe(p-CH2)SO3H as a substitute for Boc-Tyr(SO3H) in CCK8
AUTHOR(S): Gonzalez-Muniz, Rosario; Cornille, Fabrice; Bergeron, Florence; Ficheux, Damien; Pothier, Joel; Durieux, Christiane; Roques, Bernard P.
CORPORATE SOURCE: Dep. Org. Chem., UFR Pharm. Biol. Sci., Paris, 75270, Fr.
SOURCE: International Journal of Peptide & Protein Research (1991), 37(4), 331-40
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 115:50275

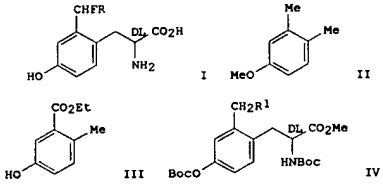
AB Substitution of the OSO3H group in the sulfated tyrosine by the nonhydrolyzable CH2SO3H group was the first described modification of the sulfate ester that does not affect CCK8 activity. In addition to its capacity to mimic the sulfated tyrosine residue, the amino acid Phe(p-CH2SO3Na) was shown to be stable in acidic media, including HF containing mixts. The synthesis of Boc-Phe(p-CH2SO3Na)-OH (Boc = Me3CO2C) in racemic and resolved forms and its introduction into the sequence of CCK8 by solid phase using standard Boc/benzyl synthesis conditions and BOP as coupling reagent is now reported. The two CCK8 analogs containing the L- or the D-Phe(p-CH2SO3Na) residue, obtained in satisfactory yields, were separated by HPLC and the stereochem. of Phe(p-CH2SO3Na) residue in each peptide was established by NMR spectroscopy and confirmed by a sep. solid-phase synthesis in which the pure L isomer was used. Both CCK8 analogs displayed high affinities for peripheral and central receptors (KI .apprx.1 nM) and proved to be full agonists in the stimulation of pancreatic amylase secretion. The "stabilized-CCK8 peptide", easily prepared by solid phase, could replace the native peptide in biochem. and pharmacol. studies. Moreover the modified amino acid Phe(p-CH2SO3Na) could also be used in solid phase synthesis to prepare a wide variety of CCK analogs and more generally, peptides analogs containing the acid-labile O-sulfated tyrosine.

IT **134790-19-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with sodium sulfite)

RN 134790-19-5 CAPLUS
CN L-Phenylalanine, 4-(chloromethyl)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:186048 CAPLUS
DOCUMENT NUMBER: 114:186048
TITLE: Syntheses of DL-2-fluoromethyl-p-tyrosine and DL-2-(difluoromethyl)-p-tyrosine as potential inhibitors of tyrosine hydroxylase
AUTHOR(S): McDonald, Ian A.; Nyce, Philip L.; Jung, Michel J.; Sabol, Jeffrey S.
CORPORATE SOURCE: Merrell Dow Res. Inst., Cincinnati, OH, 45215, USA
SOURCE: Tetrahedron Letters (1991), 32(7), 887-90
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:186048
GI



AB The title compds. I (R = H and F) were prepared from o-xylene II and benzoate III, resp. I (R = H) was obtained from II in 11 steps; a key step was the free radical bromination of tyrosine IV (Boc = Me3CO2C, R1 = H) with NBS followed by treatment with AgF to give IV (R1 = F). I (R = F) was prepared from III in 11 steps. I (R = H, F) were partially characterized as competitive inhibitors of purified bovine adrenal tyrosine hydroxylase.

IT **133409-90-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as tyrosine hydroxylase inhibitor)

RN 133409-90-2 CAPLUS
CN Tyrosine, 2-(fluoromethyl)- (9CI) (CA INDEX NAME)